An overview of modelling craniosynostosis using finite element method

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Abstract:

Craniosynostosis is a medical condition caused by the early fusion of the cranial joint. Finite element method is a computational technique that can answer a variety of "what if" questions in relation to the biomechanics of this condition. The aim of the paper was to review the current literature that has used finite element method to investigate the biomechanics of any aspect of craniosynostosis being its development or its reconstruction. This review highlighted that a relatively small number of studies (n=10) have used finite element method to investigate the biomechanics of craniosynostosis. Current studies set a good foundation for future studies to take advantage of this method and optimize reconstruction of various forms of craniosynostosis.

Keywords: biomechanics, skull growth, finite element, model validation

1- Introduction

During the early years of life, human brain volume increases rapidly and the cranium undergoes rapid morphological changes in both size and shape (Dekaban, 1977; Scheuer and Black 2004; Abbott et al., 2010). The neurocranium in particular is required to expand to provide protection for the brain (Morriss-Kay and Wilkie, 2005; Richtsmeier and Flaherty, 2013). This is accommodated by the cranial joints i.e. sutures (Opperman, 2000; Herring, 2008). Premature closure of the sutures, or craniosynostosis, is a medical condition that occurs in about 1 in 2,000 births with several reports of increase in its occurrence (van der Meulen et al., 2009; Johnson and Wilkie, 2011; Cornelissen et al., 2016; Al-Rekabi et al., 2017). The majority of cases (70%) are non-syndromic i.e. single suture synostosis, with the remaining instances being syndromic (e.g. Crouzon and Apert), in which more than one suture fuses and where additional features are present such as midfacial hypoplasia (Morriss-Kay and Wilkie, 2005; Wilkie et al., 2017).

Current treatments of this condition in the majority of cases involve invasive surgery where a multidisciplinary working group of plastic and reconstructive surgeons, neurosurgeons, anaesthestist, maxillofacial surgeons and orthodontists correct this craniofacial deformity. This group is also supported by a larger team of experts in psychology, speech and language therapy and genetics (Mathijssen, 2015). The underlying aim of the surgery is to release the pressure on the growing brain and provide the required space for it to grow while the overlying complex of bones and sutures form a protective shell. At the same time there are a large number of patient-specific factors that need to be considered during the course of craniosynostosis treatment such as age and intracranial pressure. There are a number of reconstruction techniques for different forms of craniosynostosis. These techniques have generally evolved over years in each craniofacial centre due to their experience, while ensuring the best surgical outcome for the child (e.g. McCarthy et al., 1995; Clayman et al., 2007; Thomas et al., 2015). Nonetheless, when comparing different centres' techniques for treatment of a single form of craniosynotosis there could be huge variations between them (e.g. Hopper et al., 2002; Taylor and Maugans, 2011; Simpson et al., 2017). For example, in the case of sagittal synostosis which is the most common form of craniosynostosis (Wilkie et al., 2017), there are a number of different techniques used. These range from newer techniques such as: minimally invasive endoscopic strip craniotomy with helmeting or spring-mediated cranioplasty, to other invasive calvarial reconstruction techniques such as Pi and modified Pi techniques, H technique or total cranial vault remodelling (e.g. Jimenez and Barone, 2013; Gerety et al., 2015; Simpson et al., 2017).

Calvarial reconstruction in craniosynostosis can be optimized using various computational tools. Finite element method (FEM) is a well-established tool that has been widely used to design, develop and optimize various mechanical structures such as aeroplanes and bridges (e.g. Fagan, 1992). In brief, FEM works by dividing the geometry of the problem under investigation into a finite number of sub-regions, called elements. The elements are connected together at their corners and sometimes along their mid-sides points, called nodes. For mechanical stress analysis, a variation in displacement (e.g. linear or quadratic) is then assumed through each element, and equations describing the behaviour of each element are derived in terms of the (initially unknown) nodal displacements. These element equations are then combined to generate a set of system equations that describe the behaviour of the whole problem. After modifying the equations to account for the boundary conditions applied to the problem, these system equations are solved. The output is a list of all the nodal displacements. The element strains can then be calculated from the displacements, and the stresses from the strains. This method can be then performed iteratively to optimize a particular design to achieve a certain displacement or level of strain and stress considering the loading applied to the system and its requirements.

The FEM was introduced to the field of orthopaedic trauma in 1950s (Huiskes and Chao, 1983) and is nowadays widely used in design and development of various implantable devices. Perhaps the earliest finite element analysis of the craniofacial system date back to 1970s (see e.g. Hardy and Marcal, 1973; Tanne et al., 1988; Lestrel, 1989). For example, Hardy and Marcal, (1973) developed a simplified model of skull and concluded that skull is well designed for resistance to anterior loads. There are a large number of studies that have used FEM in a wide range of application on the craniofacial system. Many studies have used FEM for example in the field of craniofacial injury and trauma with a number of studies focusing on adult as well and infant related trauma (e.g. Horgan and Gilchrist, 2003; Roth et al., 2010; Wang et al., 2016; Dixit and Liu, 2017; Ghajari et al., 2017). At the same time in the past 20 years, evolutionary biologists and functional morphologists have widely used this technique to understand the form and function of craniofacial systems in an evolutionary context (e.g. Rayfield, 2007; Moazen et al., 2009; Wang et al., 2010; O'Higgins et al., 2011; Prado et al., 2016). More recently this technique has been used to understand the biomechanics of craniofacial development and its associated congenital diseases such as cleft lip palate and craniosynostosis (e.g. Remmler et al., 1998; Pan et al., 2007; Khonsari et al., 2013; Jin et al., 2014; Lee et al., 2017; Marghoub et al., 2018).

The aim of this study was to review the current literature that have used finite element method to investigate the biomechanics of craniosynostosis in its development or its reconstruction. This review was organized to review these studies with respect to the steps involved in development of such models and to briefly describe their results. Recommendations for future research and areas which require further scientific investigation are also discussed.

2- Materials and Methods

A detail survey of literature was carried out to identify the studies that used FEM to investigate the biomechanics of craniosynostosis. A number of databases: Web of Science, SCOPUS, PubMed and Google Scholar were searched with the following keywords: craniosynostosis AND finite AND element. We identified 10 published articles that met the inclusion criteria of this review. The overall aims of these studies and type of synostosis are summarized in Table 1.

Four key steps were highlighted in the identified studies (as per any finite element study): representation of the skull, sutures and craniotomies; representation of the material properties of bones and sutures; representation of the loads; and simulation predictions. Figure 1 shows how one of these studies transformed computed tomography data of a patient with sagittal synostosis to model a reconstruction technique for treatment of this condition using finite element method (Wolanski et al., 2013). The following sections review these steps in the identified studies. These details are also summarized in Table 1 and 2.

2-1 Representation of the skull, sutures and craniotomies

Computer aided design tools have been used to simplify the morphology of the human head to geometries such as spherical, spheroidal or ellipsoidal shells. A study by Weickenmeier et al., (2017) used such an approach to model several types of craniosynostosis i.e. predicting the pre-operative calvarial morphology. On the other hand, computed tomography (CT) and magnetic resonance imaging (MRI) have also been used to develop a more detailed representation of the skull (e.g. Nagasao et al., 2010; Wolanski et al., 2013; Li et al., 2017; Borghi et al., 2018). The images are generally reconstructed using an image processing software. Some studies have only modelled craniofacial bones and craniotomies (e.g. Larysz et al., 2012; You et al., 2010; Wolanski et al., 2013; Zhang et al., 2016; Li et al., 2017) while others have also included the cranial sutures (e.g. Nagasao et al., 2011).

2-2 Representation of the material properties of bones and sutures

Bone and sutures have been generally modelled as linear, elastic materials with most of the studies using a constant value across the skull (You et al., 2010; Larysz et al., 2012; Wolanski et al., 2013; Zhang et al., 2016). Nonetheless, a wide range of elastic modulus (E) have been used to model the calvarial bones. For example, studies of Larysz et al., (2012) and Wolanski et al., (2013) used an elastic modulus of 380 MPa for bones in children aged 3-5 months and 1 year of age. Zhang et al., (2016) used an elastic modulus of 1300 MPa for infants aged 3-6 months and 6500 MPa for infants older than 6 months (see Table 1 and 2). For suture material properties, however, only one value of 3.8 MPa was reported by Nagasao et al., (2010 and 2011). Borghi et al., (2018) recently used a value of 16 MPa to model coronal and lambdoid sutures in a patient-specific model of sagittal synostosis spring assisted reconstruction.

2-3 Representation of the loads

Most of the studies considered the foramen magnum as a stationary point on the human skull during the growth (e.g. Nagasao et al., 2010 and 2011). This anatomical point has, therefore, been used as the main area of constraint for most of the FE studies. Most of the studies modelled immediate post-operative reconstruction and only loaded their models with a constant intracranial pressure (You et al., 2010; Jiang et al., 2010; Larysz et al., 2012; Nagasao et al., 2010 and 2011; Wolanski et al., 2013; Zhang et al., 2016; Li et al., 2017). The only study that modelled the calvarial growth during the development is the work of Weickenmeier et al., (2017).

2-4 Simulation predictions and accuracy

Generally, two parameters have been extracted from the results of the finite element models: (1) deformation of the skull, which has also been used to calculate the cephalic index (the maximum width to maximum length ratio multiplied by 100); (2) mechanical strain and stress within the calvarial bone.

The accuracy of finite element models depends on the choice of input parameters as well as the number of computations used to derive the solution. The number of computations is related to the number and type of elements in the model i.e. mesh convergence. Most of the studies have used the input parameters related to material properties of their models based on previous experimental studies (You et al., 2010; Nagasao et al., 2010 and 2011; Zhang et al., 2016; Weickenmeier et al., 2017; Li et al., 2017). However, they generally have not reported details of mesh convergence.

3- Results

The cases studied and their key outcomes are summarized in Table 3. In brief, studies of Nagasao et al., (2010 and 2011) mainly focused on the deformation of the orbits either preoperatively investigating the effect of different types of craniosynostosis or postoperatively investigating the effect of forehead remodelling. Studies of You et al., (2010), Jiang et al., (2010), Larysz et al., (2012) and Wolanski et al., (2013) and Li et al., (2017) compared different methods of reconstruction for sagittal and metopic synostosis. Authors virtually reconstructed the skull based on different craniotomies and commented on the skull shape immediately post-operatively and the pattern of stress and strain distribution in different reconstructions (see example from Wolanski et al., 2013 in Figure 1). Zhang et al., (2016), used finite element method to quantify the spring force in spring assisted cranioplasty for sagittal synostosis. They measure spring forces in the range of 5-8 N. A study by Weickenmeier et al., (2017) predicted calvarial growth for different types of craniosynostosis.

Overall, there was a lack of detailed validation of the FE results. For example, Weickenmeier et al., (2017) compared their modelling findings quantitatively with clinical data only in terms of the cephalic index for different types of craniosynostosis. Similarly, study of Nagasao et al., (2011) compared their FE prediction of orbital distance in three different groups (normal skull, metopic synostosis and metopic synostosis following forehead reconstruction) with their clinical data. Perhaps, the most detail validation study to date is the study of Borghi et al., (2018), who developed a patient-specific model of sagittal synostosis and compared the skull shape based on their FE predictions versus post-operative 3D head scan of the same patient's head.

4- Discussion

The current biomechanical literature relating to craniosynostosis was reviewed. Several studies were found that directly developed finite element models of craniosynostosis (n=10). Whilst these studies all highlighted the potential of finite element method to advance treatment of craniosynostosis, it is clear that there is more work to be done. Here two key areas that can be improved are discussed: (1) addressing the modelling assumptions and (2) validating the finite element results.

Firstly, there is a clear lack of detail description of the methodologies used in these studies. The technical details and how the models have been developed can be significantly improved. Here perhaps, four areas can be highlighted: (1) loading – most of the studies have applied a constant pressure to load the calvaria with exception of study of Weickenmeier et al., (2017). This approach allows for a comparison of different reconstructions at a single time point during the development. It does not, however, explain how the growing brain interacts with different calvarial reconstructions during the development. In this respect, intracranial volume or brain soft tissue can be modelled and expanded based on the changes in the intracranial volume to take into account the loading arising from the growing brain (Jin et al., 2014; Libby et al., 2017; Marghoub et al., 2018); (2) modelling the sutures – it is well established that the sutures can release the local mechanical strain (e.g. Moss, 1954; Jaslow and Biewner, 1995; Moazen et al., 2013). It is important to include the sutures to develop more realistic models of the craniofacial system (Jin et al., 2013; Weickenmeier et al., 2017; Libby et al., 2017; Marghoub et al., 2018). Sutures can be segmented during the reconstruction of the model of the skull via image processing and incorporated into the finite element simulation; (3) modelling dura mater and other soft tissues – including other soft tissues such as dura mater and muscles will evidently lead to more realistic finite element models of the skull growth. You et al., (2010) included dura mater in their model but it is not clear to us how this tissue was modelled. In this respect, head models developed to simulate head injuries include various soft tissues (e.g. Roth et al., 2010). These models can provide insights for developing more representative models of craniosynostosis (see review by Dixit and Liu, 2017). It must be noted that while increasing the complexity of FE models is possible, further studies are required to investigate how much complexity is needed to develop a validated model of craniosynostosis, whereby, the outcome of different reconstructions can be reliably predicted; (4) material properties – our understanding of changes in mechanical properties of calvarial bones and other related tissues such as dura mater during the development is still limited. Few studies have quantified such changes during the development (e.g. McPherson and Kriewall, 1980; Margulies and Thibault, 2000; Henderson et al., 2005; Coats and Margulies, 2006; Wang et al., 2014; Moazen et al., 2015). Clearly, soft tissues involved in the calvarial development are visco-elastic materials and their properties changes during the development. Most of the current studies have used linear elastic material models. It is encouraging that recent study of Borghi et al. (2018) took into account the viscoelasticity effect of bone and sutures. In this respect, the models can improve including time-dependent changes during the growth. This perhaps also requires further experimental studies.

Second, detailed validation of the finite element models is a key step to build confidence in the results of such models. To our understanding, most of the reviewed studies in this paper lack a detailed validation of their simulation. The authors are clearly conscious of the importance of validation in such models. For example, the study by Nagasao et al., (2010), compared their FE results with clinical data in terms of orbital changes in different caniosynostosis groups that they modelled. Similarly, Weickenmeier et al., (2017) compared cephalic indices of their predicated 2D and 3D craniosynostotic skull shapes and compared their results with clinical measurements. While such simple measurements are reassuring, if the CT data of the whole skull is available a full 3D comparison between the FE and *in vivo* data can be carried out (Libby et al., 2017) and provide a more comprehensive analysis of the size and shape differences. In the case of craniosynostosis and predicting the outcome of different surgical techniques, FE results need to be compared against the follow up CT data of the same child. A caveat to this is that there might be ethical or resource issues in obtaining such CT data. In this respect, (1) 3D surface scanners can provide invaluable information (e.g. Dai et al., 2017; Borghi et al., 2018); (2) *in vitro* experimental studies can also be an alternative way to validate the FE models in a simpler condition (e.g. Szwedowski et al., 2011; Toro-Ibacache et al., 2016; Libby et al., 2017).

The present study focused on the finite element models of craniosynostosis, however, there are a number of studies that have used computer aided design and three dimensional printing to visualize different reconstructions of craniosynostosis for pre-operative planning of this condition (e.g. Imai et al., 1999; Mommaerts et al., 2001; Meehan et al., 2003; Iyer et al., 2018). These studies are clearly advancing the treatment of craniosynostosis and models generated from these studies can be used to develop finite element simulations of the skull growth to predict the outcomes of different reconstructions on a virtual platform.

In summary, a few studies to date have used finite element method to optimize the reconstruction of craniosynostosis skulls. The reviewed studies clearly show the potentials of this technique, however, there are several limitations that need to be addressed in relation to their input parameters and validations. Nonetheless, they provide a strong foundation for future studies.

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Table 1: A summary of previous studies objectives, details of patient population considered.

Authors	*Aims and objectives*	*Type of synostosis/Groups*	*Patient(s)/Specimens*	*Source of geometry*
Nagasao et al. (2010)	To compare the difference in orbital deformation in patients with unicoronal synostosis between those whom only show unicoronal synostosis and those whom also show sphenoidal fusion.	• Unicoronal • Unicoronal and lambdoid	• 4.2±1.4 m/o (8 unicoronal) • 4.6±2.2 m/o (7 unicoronal and lambdoid) [Untreated, normal expansion]	i. CT
You et al. (2010) & Jiang et al., (2010)	To analyze the relationship between different craniotomies, and the overall skull rigidity in PI- shape reconstruction.	• Not specified	• Not specified [Untreated, virtual surgery]	i. CT
Nagasao et al. (2011)	To investigate how normal, pre-operative metopic and post – operative metopic craniosynostosis orbital morphology are affected by the loading from intracranial pressure.	• Metopic [untreated] • Metopic [treated] • Healthy skull (HS)	• 8.2±4.5 months (10 MS patients) • 8.6±4.3 months (10 HS patients) [Untreated and treated, normal expansion]	i. CT
Larysz et al. (2012)	To propose a method of pre-operative planning for craniosynostosis based on 3D modelling and biomechanical analysis using finite element method.	• Sagittal • Metopic	• 1 y/o, male • 3 m/o, male [Untreated, virtual surgery]	i. CT ii. MRI
Wolanski et al. (2012)	To highlight the potentials of finite element method for pre-operative planning and post-operative evaluation of patients with craniosynostosis	• Sagittal • Metopic	• 5 m/o, male (2 scenarios) • 3 m/o, male (2 scenarios) [Untreated, virtual surgery]	i. CT
Zhang et al. (2016)	To present and validate a system which accurately can predict the optimal spring force for sagittal craniosynostosis reconstruction.	• Sagittal [Spring assisted surgery]	• 3-6 m/o, unknown sex (15 patients) • >6 m/o, unknown sex (8 patients) [Virtual surgery]	i. CT ii. Laser

Table 1 continued.

Authors	***Purpose***	***Type of synostosis/Groups***	***Patient(s)***	***Source of geometry***
Weickenmeier et al. (2017)	To predict typical skull morphologies in most common forms of craniosynostosis	• Unicoronal [untreated] • Bicoronal [untreated] • Lambdoid [untreated] • Metopic [untreated] • Sagittal [untreated] • Healthy skull [untreated]	• 2D study: Cross-sectional area of newborn scaled to healthy CI value of 78 (First 4 scenarios above) • 3D study: Approximated as ellipsoid with CI of 78 (All 6 scenarios above)	i. MRI (2D) ii. CAD (3D)
Li et al. (2017)	To quantify the positive outcome of using computer assisted pre-operative planning such as biomechanical analysis and 3D printing	• Sagittal [Calvarial vault remodeling]	• 8-13 m/o, 7x male & 3x female (10 patients -Traditional treatment) • 8-13 m/o, 4x male & 4x female (8 patients - Computer assisted pre-op planning)	i. CT ii. MRI iii. Cephalograms
Borghi et al. (2018)	To develop a patient specific computational model of sprint assisted cranioplasty to predict the individual overall head shape	• Sagittal	• Pre-operative CT data at 4.4 m/o 1x male and post-operative 3D surface data at 5.5 m/o of the same patient	CT

Table 2: A summary of the material properties and boundary conditions considered in the previous studies.

Authors	***Material properties***	***Constraints***	***Loading***
Nagasao et al. (2010)	• Cortical bone: E= 134000 MPa, v=0.3 • Cancellous bone: E= 7700 MPa, v=0.3 • Cranial sutures: E= 3.78 MPa, v=0.45 [Remained constant]	• Foramen magnum – fixed in all DOF	• Intracranial pressure of 15 mm Hg was applied normal to all element of inner surface of skull.
You et al. (2010) & Jiang et al., (2010)	• Bone: E=2500 MPa, v=0.22, density=2.15 kg/cm3 • Dura matter: E=34.5MPa, v=0.45, density=1.14 kg/cm^3 [Remained constant]	• Posterior distal edge of parietal bone – fixed in all DOF	• Intracranial pressure of 2kPa (15mm Hg) was applied normal to all element of inner surface of skull.
Nagasao et al. (2011)	• Cortical bone: E=134000 MPa, v=0.3 • Cancellous bone: E=7700 MPa, v=0.3 • Cranial suture: E=3.78 MPa, v=0.45 [Remained constant]	• Foramen magnum – fixed in all DOF	• Intracranial pressure of 15 mm Hg was applied normal to all element of inner surface of skull.
Larysz et al. (2012)	• Bone: E=380 MPa (based on radiological density in Hounsfield Units) [Remained constant]	• Not specified.	• Not clear to us.
Wolanski et al. (2012)	• Bone: E=380MPa, v=0.22 [Remained constant]	• Fixed – base of skull	• Intracranial pressure of 2.66 kPa (19.95 mm Hg) was applied normal to all element of inner surface of skull. • Applied deformation based on re-modelling of skull
Zhang et al. (2016)	• Bone: E=1300 MPa, v=0.28 - (Group A) • Bone: E=6500 MPa, v=0.22 - (Group B) [Remained constant]	• Opposite edge of spring fixed	• Point loading force at spring contact region (Initial value of 6.9 N)
Weickenmeier et al. (2017)	• Not specified.	**2D:** Fixed at the center and kinematic constraint on sutures **3D:** Center fixed and corresponding suture region depending on scenario	**2D:** Unidirectional homogeneous expansion **3D:** Orthotropic in-plane growth: Length. Width and Bidirectional loading (Simulates 12 months growth, 30% increase in circumference)

Table 2 continued.

Authors	***Material properties***	***Constraints***	***Loading***
Li et al. (2017)	• Bone – details are not specified. • Fixation device - details are not specified	• Not specified.	• Not specified.
Borghi et al. (2018)	• Bone: E=421 MPa, v=0.22 • Sutures: E=16 MPa, v=0.49 The viscoelasticity of both bone and sutures were modelled through Prony shear and bulk relaxation relationship.	• Model was constrain at the distal end of three quarter of the skull (in the transverse plane) to avoid free expansion of the head base in this plane.	• Spring expansion was simulated.

Table 3: A summary of results of current finite element analysis of craniosynostosis. NA abbreviate "not applicable".

Authors	***Presented data***	***Validation***	***Outcome***
Nagasao et al. (2010)	• Orbital deformation around the eye socket	Quantitative analysis of clinical data	• Results showed that only frontoparietal synostosis caused more deformation around the orbit compare to combined frontoparietal and frontosphenoidal synostosis. • Degree of fusion presented by frontosphenoidal synostosis should be evaluated in detail
You et al. (2010) & Jiang et al., (2010)	• FE Stress & displacement on different craniotomies for Pi-shaped operation	NA	• Results indicated that cranial bone rigidity is a key factor with profound influence on post-op. outcomes and lower bone rigidity leads to better results (Schemes 4-5). • No validation of the research was provided to support these results/claims
Nagasao et al. (2011)	• Orbital deformation around eye socket for normal skulls, untreated and treated metopic synostosis skulls	Quantitative analysis of clinical data	• Results showed expansion of interorbital distances due to intracranial pressure is constrained structurally in metopic synostosis. The remodeling of the frontals during metopic synostosis treatment allows the expansion of the frontals. This then increases the interorbital distance and improve the facial morphology.
Larysz et al. (2012)	• FE stress and deformation on critical sections of skull following endoscopic surgical cuts	NA	• Pattern of skull deformation following patient-specific metopic and sagittal synostosis calvarial reconstruction were presented. Authors also presented bone thickness and the loading levels required to cut the calvarial bones.
Wolanski et al. (2012)	• FE stress and displacement of cranium following virtual surgery	Qualitative analysis of clinical data	• Results showed that in metopic reconstruction remodelling of the forehead by one incision along the metopic and two incisions along the coronal sutures showed higher maximum displacement comparing to the same craniotomies with additional two incisions in the middle of each half of the frontal bones. • Results showed that in sagittal reconstruction inverted modified pi procedure with half-incisions in the middle of the parietal bone showed lower maximum displacement comparing to the same craniotomy with full incision in the parietal bone. Note skulls were loaded with intracranial pressure.
Zhang et al. (2016)	• Optimal spring force based on pre-operative patient-specific properties	Quantitative analysis of clinical data	• Development of a computer platform capable of predicting optimal spring force in Spring-assisted surgery (SAS) for sagittal sysnotosis. • In vivo and clinical data results indicated that bone thickness and spring force play a crucial role in surgical outcome.
Weickenmeier et al. (2017)	• CI values for various simulated craniosynostosis models in 2D and 3D	Quantitative analysis of clinical data	• Typical craniosynostotic skull shapes were predicted using simplified 2D and 3D elliptical models. • The cephalic index predictions based on the 2D model showed 0.5% to 12% difference with clinical data across sagittal, lambdoid, metopic, uni/bi coronal synostosis. The 3D model showed 0.5% to 3.5% difference between the predicted and clinical cephalic indexes.

Table 3: continued.

Authors	*Presented data*	*Validation*	*Outcome*
Li et al. (2017)	• Surgical data such as time, blood loss, cost and CI values were measured and compared	Qualitative analysis of clinical data	• Presented stress and strain analysis of a single case for sagittal synosotsis reconstruction. • Quantitative data i.e. operative duration, blood loss, hospital cost pre & post-operative cephalic indexes were also presented comparing a preoperative planning cohort versus a non-pre-operative planning cohort.
Borghi et al. (2018)	• Spring opening over time and predicted calvarial shape following surgery.	Quantitative comparison versus 3D surface data obtained from a handheld scanner.	• A validated patient-specific model of spring assisted sagittal synostosis was developed. • Highlighted the potentials of finite element method to predict the skull shape of craniosynostotic patients following surgery.

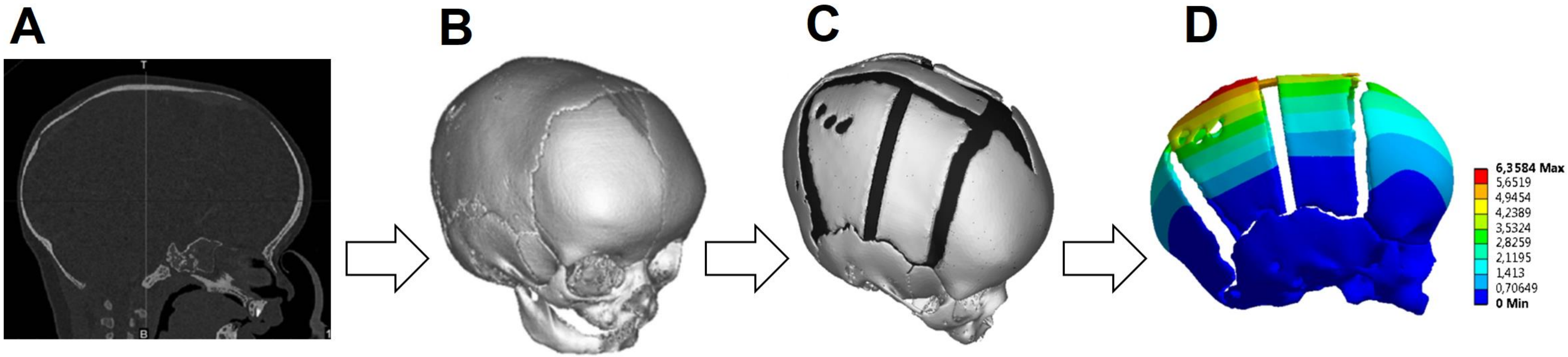

Figure 1: A summary of model development from (A) computed tomography to (B) 3D reconstructed model of the skull pre-operatively to (C) then 3D virtual reconstruction post-operatively and then to (D) finite element predictions, here due to constant pressure applied to the inner surface of the skull (modified with permission from Wolanski et al., 2013).